
Genetically encoding unnatural amino acids for cellular and neuronal studies.

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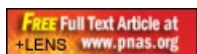
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Public Summary:

Scientific Abstract:

Proteins participate in various biological processes and can be harnessed to probe and control biological events selectively and reproducibly, but the genetic code limits the building block to 20 common amino acids for protein manipulation in living cells. The genetic encoding of unnatural amino acids will remove this restriction and enable new chemical and physical properties to be precisely introduced into proteins. Here we present new strategies for generating orthogonal tRNA-synthetase pairs, which made possible the genetic encoding of diverse unnatural amino acids in different mammalian cells and primary neurons. Using this new methodology, we incorporated unnatural amino acids with extended side chains into the K⁺ channel Kv1.4, and found that the bulkiness of residues in the inactivation peptide is essential for fast channel inactivation, a finding that had not been possible using conventional mutagenesis. This technique will stimulate and facilitate new molecular studies using tailored unnatural amino acids for cell biology and neurobiology.

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